## I. AMENDMENTS TO THE SPECIFICATION

Please amend the specification as follows, where underlining indicates insertion, and ~~strikeout~~ or double brackets, "[[ ]]," indicate deletion:

Please amend paragraphs **[0014]** to **[0016]** as follows:

**[0014]** The term "water-insoluble polymers" refers to polymers suitable for use in coating pharmaceutically acceptable solid dosage forms. Water-insoluble polymers suitable for use in the methods and coated solid dosage forms of the present invention include cellulose esters such as mono-, di- and triacylates including mixed esters such as, for example, cellulose acetate, cellulose diacetate, cellulose triacetate, cellulose propionate, cellulose acetate butyrate, cellulose acetate propionate, cellulose tripropionate; cellulose ethers such as ethyl cellulose; nylons; polycarbonates; poly(dialkylsiloxanes); poly(methacrylic acid) esters; poly(acrylic acid) esters; poly(phenylene oxides); poly(vinyl alcohols); aromatic nitrogen-containing polymers; polymeric epoxides; regenerated cellulose; membrane-forming materials suitable for use in reverse osmosis or dialysis application; agar acetate; amylose triacetate; beta glucan acetate; acetaldehyde dimethyl acetate; cellulose acetate methyl carbamate; cellulose acetate phthalate; cellulose acetate succinate; cellulose acetate dimethylamino acetate; cellulose acetate ethyl carbonate; cellulose acetate chloroacetate; cellulose acetate ethyl oxalate; cellulose acetate propionate; poly(vinylmethylether) copolymers; cellulose acetate butyl sulfonate; cellulose acetate octate; cellulose acetate laurate; cellulose acetate p-toluene sulfonate; triacetate of locust gum bean; hydroxylated ethylene-vinyl acetate; cellulose acetate butyrate; wax or wax-like substances; fatty alcohols; shellac; zein; hydrogenated vegetable oils; SURELEASE®~~Surelease®~~ (Colorcon, Westpoint, PA, U.S.A.) E-7-19010 aqueous ethylcellulose dispersion; and the like, and combinations thereof. The water-insoluble polymer is preferably ethylcellulose or SURELEASE® E-7-19010 aqueous ethylcellulose dispersion ~~Surelease®~~.

**[0015]** The term "water-soluble pore former" refers to pharmaceutically acceptable material that forms pores, or channels in a coating layer, when incorporated therein. The water-soluble pore former included in the coating solution used to produce

the coating of the coated solid dosage forms of the present invention is preferably particulate in nature, with an average particle size from about 0.1 to about 200 μm. In order to be suitable for use in the present invention, the water-soluble pore former must be soluble in water or aqueous media and insoluble in the organic solvent in which the water-insoluble polymer is dissolved during the film-coating process. Suitable pore formers include, alkali metal salts such as, for example, magnesium sulfate, magnesium chloride, magnesium succinate, citric acid, lithium chloride, lithium sulfate, lithium carbonate, sodium carbonate, sodium chloride, sodium bromide, sodium sulfate, sodium acetate, sodium citrate, calcium chloride, calcium bicarbonate, calcium lactate, potassium chloride, potassium sulfate, potassium phosphate, and the like, and mixtures thereof; water soluble hydrophilic polymers such as, for example, cellulose ethers, hydroxypropylcellulose, hydroxypropyl methylcellulose (hereinafter, "HPMC"), hydroxypropylmethylcellulose phthalate, sodium carboxymethylcellulose, protein-derived materials, polyvinylpyrrolidone, cross-linked polyvinylpyrrolidone, polyethylene oxide and water-soluble polydextrose; and saccharides and polysaccharides, such as, for example, pullulan, dextran, sucrose, glucose, fructose, mannitol, lactose, mannose, galactose, and sorbitol~~, Opadry® (Colorcon, Westpoint, PA, U.S.A.)~~ and the like, and mixtures thereof. The pore former is preferably HPMC ~~or Opadry®~~.

**[0016]** The coating solution used in coating the solid dosage form according to the method of the present invention comprises a water-insoluble polymer and a water-soluble polymer. In one preferred embodiment, the coating solution comprises OPADRAY® (Colorcon, Westpoint, PA, U.S.A.) ~~Opadry®~~ and ethylcellulose. OPADRY® is a film coating system comprised of HPMC and polyethylene glycol, hereinafter referred to as "OPADRY® HPMC film coating." In another preferred embodiment, the coating solution comprises SURELEASE® E-7-19010 aqueous ethylcellulose dispersion ~~Surelease®~~ and OPADRY® HPMC film coating ~~Opadry®~~. The coating solution is applied to the solid dosage form by methods well known to persons having ordinary skill in the art, such as spray coating.

Please amend all the paragraphs of the Examples section as follows:

EXAMPLE 1

[000~~1~~33] Compressed tablets of pramipexole were prepared according to the following procedure, using tablet core ingredient amounts set forth in Examples 2-5, below.

[000~~2~~34] 1. All tablet core ingredients (i.e., pramipexole, HPMC 2208 4000 cps, pregelatinized starch, colloidal silicon dioxide, and magnesium stearate) were passed through a pharmaceutical screen of about a 30 mesh.

[000~~3~~35] 2. All the tablet core ingredients except magnesium stearate were dry mixed at about 24 rpm for about 10 to about 30 minutes in a low shear mixer (a V blender or bin blender).

[00[[04]]36] 3. The magnesium stearate was weighed and combined in the blender with the remainder of the mixture from step 3, and mixed for an additional 2 to 5 minutes.

[000~~5~~37] 4. Samples of the resulting mixture from step 4 were compressed into tablets, using a tablet press.

[000~~6~~38] 5. The compressed tablets were then coated and cured, as described in Examples 2-5, below.

EXAMPLE 2

[000~~7~~39] Compressed pramipexole tablets were prepared as described in Example 1, above, using the amounts of tablet core ingredients shown in Table 1, below; and coated with a coating solution comprising ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion and about 25% by weight ~~pore-former (Opadry®)~~ OPADRY® HPMC film coating, as described herein below.

[0040]

**Table 1**

| Component | Amount (mg) | % by Weight |
|---|---|---|
| Pramipexole | 0.375 | 0.1 |
| HPMC 2208 4000 cps | 140 | 38.8 |
| Pregelatinized Starch | 206.48 | 57.3 |
| Colloidal Silicon Dioxide | 1.4 | 0.4 |
| Magnesium Stearate | 1.75 | 0.5 |
| ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion | 7.88 | 2.2 |
| ~~Opadry®~~OPADRY® HPMC film coating | 2.63 | 0.7 |
| Total | 360.5 | 100 |

[003~~3~~41] The coating solution used in this Example was prepared, first, by adding 6.0037 g ~~Opadry®~~OPADRY® HPMC film coating to 106.682 g water, and mixing for 45 minutes. 72.045 g ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion was then added to the ~~Opadry®~~ OPADRY® HPMC film coating mixture and mixed for an additional 30 minutes to provide the coating solution.

[00[[34]]42] The coating solution was applied to the compressed tablets, for a theoretical weight gain of about 3%. Table 1 shows the amount of ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion and ~~Opadry®~~ OPADRY® HPMC film coating applied to each tablet for a theoretical weight gain of about 3% per tablet, in this step of the present procedure.

[003~~5~~43] The coated tablets were then cured using either a Vector LCDS coating pan or a Thomas Accela-Cotta coating pan for about 15 minutes at a bed temperature of at least about 70°C. After curing, the temperature was ramped down over a period of about 8 minutes to an exhaust temperature of about 45°C.

EXAMPLE 3

[000844] Compressed pramipexole tablets were prepared as described in Example 1, above, using the amounts of tablet core ingredients shown in Table 1, below; and coated with a coating solution comprising ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion and about 20% by weight ~~pore former (Opadry)~~ OPADRY® HPMC film coating, as described herein below.

[0045]

**Table 2**

| Components | Amount (mg) | % by Weight |
|---|---|---|
| Pramipexole | 0.375 | 0.1 |
| HPMC 2208 4000 cps | 140 | 38.8 |
| Pregelatinized Starch | 206.48 | 57.3 |
| Colloidal Silicon Dioxide | 1.4 | 0.4 |
| Magnesium Stearate | 1.75 | 0.5 |
| ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion | 8.4 | 2.3 |
| ~~Opadry®~~ OPADRY® HPMC film coating | 2.1 | 0.6 |
| Total | 360.5 | 100 |

[003646] The coating solution used in this Example was prepared, first, by adding 4.8012 g OPADRY® HPMC film coating ~~Opadry®~~ to 103.04114 g water, and mixing for 45 minutes. 76.8192 g ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion was then added to the ~~Opadry®~~ OPADRY® HPMC film coating mixture and mixed for an additional 30 minutes to provide the coating solution.

[003747] The coating solution was applied to the compressed tablets, for a theoretical weight gain of about 3%. Table 2, above, shows the amount of ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion and ~~Opadry®~~ OPADRY® HPMC film coating applied to each tablet for a theoretical weight gain of about 3% per tablet, in this step of the present procedure.

[003848] The coated tablets were then cured using either a Vector LCDS coating pan or a Thomas Accela-Cotta coating pan for about 15 minutes at a bed temperature of at least about 70°C. After curing, the temperature was ramped down over a period of about 8 minutes to an exhaust temperature of about 45°C.

EXAMPLE 4

[003949] Compressed pramipexole tablets were prepared as described in Example 1, above, using the same amounts of each tablet core ingredient per tablet as were used in the tablets produced as described in Example 2, above. As in Example 2, the tablets were also coated with a coating solution comprising ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion and about 25% by weight ~~pore former (Opadry®)~~ OPADRY® HPMC film coating. However, in the present Example, the tablets were coated and cured twice. The amount of each component used in each tablet prepared as described below, is shown in Table 3:

[0050]

**Table 3**

| Components | Amount (mg) |
|---|---|
| Pramipexole | 0.375 |
| HPMC 2208 4000 cps | 140 |
| Pregelatinized Starch | 206.48 |
| Colloidal Silicon Dioxide | 1.4 |
| Magnesium Stearate | 1.75 |
| ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion | 13.13 |
| ~~Opadry®~~ OPADRY® HPMC film coating | 4.38 |
| Total | 367.5 |

[00[[40]]51] The coating solution used in this Example was prepared, first, by adding about 10.0025 g OPADRY® HPMC film coating ~~Opadry®~~ to about 177.7367 g water and mixing for about 45 minutes. About 120.03 g ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion was then added to the ~~Opadry®~~ OPADRY®

HPMC film coating mixture and mixed for an additional 30 minutes to provide a coating solution. The coating solution was applied to the compressed tablets for a theoretical weight gain of about 3%.

[00[[41]]52] The coated tablets were then cured using a Vector LCDS coating pan (12") or a Thomas Accela-Coata coating pan (24") for about 15 minutes at a bed temperature of at least above 70°C. After curing, temperature was ramped down over a period of about 8 minutes to an exhaust temperature of about 45°C.

[00[[42]]53] The coating step was then repeated for a total tablet weight gain of about 5%, followed by curing for about 15 minutes at a bed temperature of at least about 70°C. After curing, temperature was ramped down over a period of about 8 minutes to an exhaust temperature of about 45°C.

EXAMPLE 5

[00[[43]]54] Compressed pramipexole tablets were prepared as described in Example 1, above, using the same amounts of each tablet core ingredient per tablet as were used in the tablets produced as described in Example 3, above. As in Example 3, the tablets were also coated with a coating solution comprising ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion and about 20% by weight ~~pore former (Opadry®)~~ OPADRY® HPMC film coating. However, in the present Example, the tablets were coated and cured in two steps. The amount of each component used in each tablet prepared as described in the present Example is shown in Table 4:

[0055]

**Table 4**

| Components | Amount (mg) |
|---|---|
| Pramipexole | 0.375 |
| HPMC 2208 4000 cps | 140 |
| Pregelatinized Starch | 206.48 |
| Colloidal Silicon Dioxide | 1.4 |
| Magnesium Stearate | 1.75 |
| ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion | 14.0 |
| ~~Opadry®~~ OPADRY® HPMC film | 3.5 |

| | |
|---|---|
| coating | |
| Total | 367.5 |

[00[[44]]56] The coating solution used in this Example was prepared, first, by adding 8.002 g ~~Opadry®~~ OPADRY® HPMC film coating to 171.7352 g water and mixing for 45 minutes. 128.032 g ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion was then added to the resulting mixture and mixed for an additional 30 minutes to provide a coating solution.

[00[[45]]57] The coating solution was applied to tablets for a theoretical weight gain of 3% per tablet, followed by curing, cooling, and a second coating step, for a total theoretical weight gain of about 5% per tablet, using the same coating, curing, and cooling procedure described in Example 4, above.

EXAMPLE 6

[00[[46]]58] Coated compressed tablets of pramipexole are produced as described in Example 1, using the same proportions of tablet core ingredients as are described in any one of Examples 2-5, above, and coated with the same coating mixture set forth in said Example.

[00[[47]]59] In the present Example, the tablets are coated in a single coating step for a theoretical weight gain of about 5%. The tablets are then cured and cooled as described in Examples 2 or 3, above.

[00[[48]]60] The resulting tablets are found to contain imperfections in the tablet coating, such as blisters or cracks or a combination of the two. Such imperfections were not found to be present in any of the tablets produced according to Examples 2-5, above.

EXAMPLE 7

[00[[49]]61] The four different types of coated tablets of pramipexole produced as described in Examples 2-5 (3% coating with 25% pore former, 3% coating with 20% pore former, 5% coating with 25% pore former, and 5% coating with 20% pore former), were tested for release rate over time, in an aqueous solution of pH 6.8. A plot of the release rate results is set forth in Figure 1, below.

[0050~~6~~2] Figure 1 shows that each of the four types of coated tablets tested showed an extended rate of release of pramipexole, even after 24 hours. However, the two types of tablets with 5% coating had a significantly slower rate of release compared to those with only a 3% coating. The tablets with only 20% pore former and about a 5% coating produced the slowest release rate of all the tablet types tested.

EXAMPLE 8

[0051~~6~~3] Various batches of compressed tablets of clindamycin HCl were prepared, using a roller-compaction procedure. A 20 mesh screen was used to screen all tablet core ingredients used to make the compressed tablets (i.e., clindamycin HCl, Ethocel, and magnesium stearate). The amounts of each component used in the production of each such tablet, and the procedure used to coat and cure each such tablet is set forth in Examples 9-11, below.

EXAMPLE 9

[0052~~6~~4] Compressed clindamycin HCl tablets were produced as described in Example 8, above, using the amounts of tablet core ingredients shown in Table 5, below:

[0065]

**Table 5**

| Components | Amount (mg) |
|---|---|
| Clindamycin HCl | 651.5 |
| Ethocel Std. 10 Premium FP Ethylcellulose | 207.59 |
| Magnesium Stearate NF Powder Food Grade-V-Bolted | 4.44 |
| HPMC 2910 USP 3 CPS | 6.9 |
| ~~Surelease®~~ SURELEASE® Clear Grade E-7-19010 aqueous ethylcellulose dispersion | 27.6 |
| Total | 898.03 |

[0053~~6~~6] The compressed clindamycin HCl tablets were coated with a coating solution comprising ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion and about 20% HPMC, a pore former, in the amounts shown in Table 5, for a

total theoretical weight gain of about 4%. The coating was applied in two steps, with curing and cooling steps used after each coating step, in a similar way as is described in Examples 2-5 following each coating step. Coating solution was applied for about a 2% weight gain in each of the two coating steps.

EXAMPLE 10

[005467] Compressed clindamycin HCl tablets were produced as described in Example 8, above, using the amounts of tablet core ingredients shown in Table 6, below:

[0068]

**Table 6**

| Components | Amount (mg) |
|---|---|
| PNU-21251F Clindamycin HCl | 651.5 |
| Ethocel Std. 10 Premium FP Ethylcellulose | 207.59 |
| Magnesium Stearate NF Powder Food Grade-V-Bolted | 4.44 |
| Hydroxypropyl Methylcellulose 2910 USP 3 CPS | 10.4 |
| ~~Surelease®~~ SURELEASE® Clear Grade E-7-19010 aqueous ethylcellulose dispersion | 41.4 |
| Total | 915.33 |

[005569] The compressed clindamycin HCl tablets were coated with a coating solution comprising ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion and about 20% HPMC, in the amounts per tablet shown in Table 6, for a total theoretical weight gain of about 6%. The coating was applied in three steps of 2% coating each, with curing and cooling steps similar to those described in Examples 2-5 following each coating step.

EXAMPLE 11

[005670] Compressed clindamycin HCl tablets were produced as described in Example 8, above, using the amounts of tablet core ingredients shown in Table 7, below:

[0071]

**Table 7**

| Components | Amount (mg) |
|---|---|
| PNU-21251F Clindamycin HCl | 651.5 |
| Ethocel Std. 10 Premium FP Ethylcellulose | 207.59 |
| Magnesium Stearate NF Powder Food Grade-V-Bolted | 4.44 |
| Hydroxypropyl Methylcellulose 2910 USP 3 CPS | 12.1 |
| ~~Surelease®~~ SURELEASE® Clear Grade E-7-19010 | 48.4 |
| Total | 924.03 |

[005~~7~~72] The compressed clindamycin HCl tablets were coated with a coating solution comprising ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion and about 20% HPMC, in the amounts per tablet shown in Table 6, for a total theoretical weight gain of about 6%. The coating was applied in three steps of 2% coating each, with curing and cooling steps similar to those described in Examples 2-5 following each coating step.

EXAMPLE 12

[005~~8~~73] Coated compressed clindamycin HCl tablets produced as described in Examples 10 and 11 were found to have a release rate that was so slow as to have limited utility as a drug release agent. Several additional samples of coated compressed clindamycin HCl tablets were produced using coating mixtures comprising ~~Surelease®~~ SURELEASE® E-7-19010 aqueous ethylcellulose dispersion and either 40% or 50% pore former (HPMC), for a total weight percent of coating of either 4% or 6%. The same amounts of tablet core ingredients were used as were used in Examples 9-10, above. Except for one set of tablets produced with 6% coating and 40% pore former, all of the tablets were coated and cured three times, in the same way as described in Examples 9-10.

[005974] Coated tablets were also produced with a coating for a theoretical weight gain of 6%, and coated only a single time. However, the coatings of this last set of tablets were found to have imperfections, such as blisters or cracks, or both. These tablets were not included in the release rate study, described below.

[006075] A clindamycin HCl release rate study was then conducted on all but the single step cured tablets produced as described above. The tablets were each placed in an aqueous phosphate buffer solution, with a pH of 6.8, and the amount of clindamycin HCl released into the solution was measured at various time points. A plot of the study results is shown in Figure 2, below. Figure 2 shows that tablets with about 6% coating and about 40% pore former had a steady, slow, release rate, releasing about 80% of the clindamycin by about 13 hours into the study, while the 4% coated 40% pore former cured formulation had 80% release between 8 and 9 hours, the 6% coated 50 % pore-former had 80% release at 8 hours, and all of the other tablets achieved 80% release at about 5.5 hours.. Surprisingly, the tablets with 6% and 4% uncured coating (with about 40% pore former) had the same release rate as one another, the fastest and least extended release rate of any of the coated tablets tested.